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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,754	08/24/2001	Samuel J. Danishefsky	2003080-0083 (SK-943-US)	4106
24280	7590	04/25/2005	EXAMINER	
CHOATE, HALL & STEWART LLP EXCHANGE PLACE 53 STATE STREET BOSTON, MA 02109			COLEMAN, BRENDA LIBBY	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 04/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/938,754

Applicant(s)

DANISHEFSKY ET AL.

Examiner

Brenda L. Coleman

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 7-22, 24-28, 30, 33-35, 38, 57, 58 and 63-74 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 22, 24-28, 57, 58 and 67-70 is/are allowed.
- 6) ☒ Claim(s) 1, 7, 9, 10, 12-14, 19-21, 30, 33, 38, 73 and 74 is/are rejected.
- 7) ☒ Claim(s) 2, 3, 8, 11, 15-18, 34, 35, 63-66, 71 and 72 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-3, 7-22, 24-28, 30, 33-35, 38, 57, 58 and 63-74 are pending in the application.

This action is in response to applicants' amendment filed January 14, 2005. Claims 1, 20, 30, 33, 38, 65, 66 and 72 have been amended and claims 59, 61 and 62 have been canceled.

Response to Amendment

Applicant's amendments filed January 14, 2005 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 30, 33-35, 38, 59, 61-66 and 71-74 labeled paragraph 1 maintained in the last office action, the applicants' arguments have been fully considered, however they were not found persuasive. Applicants' stated that the claims have been amended to recite particular cancers for which there is support in the present application, however, this is not so in claims 73 and 74.

Claims 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 102(b) rejection of claims 1, 13, 18, 21, 30, 33-35, 38, 59, 61, 62, 73 and 74, labeled paragraph 2 maintained in the last office action, which is hereby **withdrawn**.

3. With regards to the 35 U.S.C. § 112, second paragraph rejections labeled f) maintained in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

f) The applicants' stated that the claims have been amended to recite particular cancers, however, this is not so in claims 73 and 74.

Claims 73 and 74 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

In view of the amendment dated January 14, 2005, the following new grounds of rejections apply:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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4. Claims 1, 13, 14, 21, 30, 33, 38, 73 and 74 are rejected under 35 U.S.C. 102(a) as being anticipated by INO et al., WO 99/55689. INO teaches the compounds, compositions and method of use of the compounds of formula where X is O; Z is O; A-B is oxireno; D-E is CH=CH; G-J is CH=CH; R₁ is Cl; R₃ is H; R₂ and R₄ are OH or tert-butyl dimethylsilyl; and K-L is heteroaryl[alkyl] substituted heteroaliphatic such as examples 1, 3, 4, 5, 6, 12; cycloalkyl substituted heteroaliphatic such as example 2; pyrid-4-yl-C(=O)- substituted heteroaliphatic such as example 7; MeHNC(=O)- substituted heteroaliphatic such as example 8; t-butyl-O-C(=O)- substituted heteroaliphatic such as example 9; benzyl-O-C(=O)- substituted heteroaliphatic such as example 10; heteroaliphatic such as example 11, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37; substituted heteroarylalkyl such as examples 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26; as shown in the tables on pages 24-28 and heteroaliphatic as shown by formula K on page 63.

Applicants are reminded of the overlap in the interpretation of each of the moieties in the definitions as claimed herein. It is acknowledged that the proviso labeled (3) appears to exclude some of the examples outlined above however, substituted alkyl such as formula K where K-L is C=NOCH₂CH₂OH, i.e. a hydroxyl substituted ethyl is also interpreted as the heteroaliphatic where a CH₂ group is replaced by a hetero atom, i.e. CH₂CH₂**CH**₂H becomes CH₂CH₂OH when the bold CH₂ group is replaced with an oxygen atom, thus these compounds are still anticipated.

5. Claims 1, 13, 14, 21, 30, 33, 38, 73 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by INO et al., WO 98/18780 (U.S. equivalent 6,239,168). INO

teaches the compounds, compositions and method of use of the compounds of formula where X is O; Z is O; A-B is oxireno or $\text{CHR}_5\text{-CHR}_6$ where R_6 is halogen; R_5 is OR_J ; D-E is CH=CH ; G-J is CH=CH ; R_1 is Cl; R_3 is H; R_2 and R_4 are OH, O-alkanoyl, O-alkenoyl, tert-butyldimethylsilyl-O- or tert-butyldiphenylsilyl-O- as set forth in the proviso labeled (3); however the definition of K-L is up to interpretation as outlined above in the rejection over WO 99/55689 such that K-L can be interpreted to be optionally substituted heteroarylalkyl such as compounds 51, 52, 53, 54, 55, 56, 57, 58, 59; optionally substituted arylalkyl such as compounds 43, 44, 45, 46, 47, 48, 49, 50; etc. as shown in the table 1.

6. Claims 1, 9, 13, 19, 21, 30, 33, 38, 73 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by SHIBATA et al., JP 09-202781. SHIBATA teaches the compounds, compositions and method of use of the compounds of formula where X is O; Z is O; A-B is $\text{CHR}_5\text{-CHR}_6$ where R_6 is Cl or OH; R_5 is OH; D-E is CH=CH ; G-J is CH=CH ; R_1 is Cl; R_3 is H; R_2 and R_4 are OH. See examples 2 and 3 in the table on page 2.

7. Claims 1, 13, 14, 21, 30, 33, 38, 73 and 74 are rejected under 35 U.S.C. 102(a) as being anticipated by AGATSUMA et al., U.S. Patent No. 5,977,165. AGATSUMA teaches the compounds, compositions and method of use of the compounds of formula where X is O; Z is O; A-B is oxireno; D-E is CH=CH ; G-J is CH=CH ; R_1 is Cl; R_3 is H; R_2 and R_4 are OH or tert-butyldimethylsilyl-O- as set forth in the proviso labeled (3); however the definition of K-L is up to interpretation as outlined above in the rejection

over WO 99/55689 such that K-L can be interpreted to be heteroaliphatic such as compounds 12, 13; $\text{CH}_2=\text{CH}-\text{CH}_2-\text{O}-\text{C}(=\text{O})$ - substituted heteroaliphatic such as compound 27; etc. as shown in the table 1 (1) and 1 (2).

8. Claims 1, 7, 9, 10, 13, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by AYER et al., *Phytochemistry*. AYER teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is oxireno, $\text{CH}=\text{CH}$ or $\text{CHR}_5-\text{CHR}_6$ where R_6 is H, or OH and R_5 is H or OH; D-E is $\text{CHR}_8-\text{CHR}_9$ where R_8 is H and R_9 is H; G-J is $\text{CHR}_{10}-\text{CHR}_{11}$ where R_{10} is H and R_{11} is H or $\text{CH}=\text{CH}$; R_1 is H; R_3 is H; R_2 and R_4 are OH; and K-L is $\text{C}(=\text{O})$ as shown by compounds 3, 4, 5, 6, 9 and 10.

9. Claims 1, 7, 9, 10, 13, 19, 21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by AYER et al., *Canadian Journal of Microbiology*. AYER teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is oxireno, $\text{CH}=\text{CH}$ or $\text{CHR}_5-\text{CHR}_6$ where R_6 is H and R_5 is OH or $\text{OC}(=\text{O})\text{Ph}$; D-E is $\text{CHR}_8-\text{CHR}_9$ where R_8 is H and R_9 is H or $\text{CH}=\text{CH}$; G-J is $\text{CHR}_{10}-\text{CHR}_{11}$ where R_{10} is H and R_{11} is H or $\text{CH}=\text{CH}$; R_1 is H or Cl; R_3 is H; R_2 and R_4 are OH or OMe; and K-L is $\text{C}(=\text{O})$ as shown by compounds 3, 4, 5, 6, 8, 10, 11 and 12.

10. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by ROBERTSON, U.S. Patent No. 4,088,658. ROBERTSON teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is $\text{CHR}_5-\text{CHR}_6$ where R_6 is H and R_5 is H; D-E is $\text{CHR}_8-\text{CHR}_9$ where R_8 is H and R_9 is H; G-J is $\text{CHR}_{10}-\text{CHR}_{11}$ where R_{10} is H and R_{11} is H; R_1 is H; R_3 is H; R_2 is H, OH or

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OSO₂Me; R₄ is H, OH, OSO₂Me or OCH₂Ph; and K-L is CH₂ as shown by compounds IA, IIA, IIIA and V.

11. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by HIDY et al., U.S. Patent No. 4,035,504. HIDY teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H; R₃ is H; R₂ is OH, OMe or OAc; R₄ is H, OH, OMe or OAc; and K-L is CH₂ as shown by compounds VII, VIII, IX, X and XI.

12. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by URRY et al., U.S. Patent No. 3,901,921. URRY teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H; R₃ is H; R₂ is OH or Obenzyl; R₄ is OH or Obenzyl; and K-L is CH₂ as shown by compounds XX and XXI in Example 21.

13. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by WEHRMEISTER et al., U.S. Patent No. 3,764,614.

WEHRMEISTER teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is

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H; R₁ is H or Cl; R₃ is H or Cl; R₂ is OH, OMe or OEt; R₄ is OH, OMe, OEt or OAc; and K-L is CH₂ as shown by compounds I, II, III, IV and V.

14. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by WEHRMEISTER et al., U.S. Patent No. 3,751,431.

WEHRMEISTER teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H or Br; R₃ is H or Br; R₂ is OH, OMe or OEt; R₄ is OH, OMe, OEt or OAc; and K-L is CH₂ as shown by compounds I, II, III, IV and V.

15. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by BROOKS et al., Proceedings of the Society for Experimental Biology. BROOKS teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H, C(=O)H or C(=O)OH and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H; R₃ is H; R₂ is OH; R₄ is OH; and K-L is CH₂ as shown by compounds in the CAPLUS printout herein provided.

16. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by JENSEN et al., U.S. Patent No. 3,621,036. JENSEN teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is C(=O)H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H; R₃ is H; R₂ is OH, OMe,

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OAc, OEt, OC(=O)Et or OCH₂Ph; R₄ is OH, OMe or OAc; and K-L is CH₂ as shown by compounds 3, 15, 16, 17, 18, etc.

17. Claims 1, 7, 9, 12, 19-21, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by WEHRMEISTER et al., Journal of Organic Chemistry.

WEHRMEISTER teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is H; R₃ is H; R₂ and R₄ are H, OH or 2-benzoxazolyloxy; and K-L is CH₂ as shown by compounds 2, 10a and 10b.

18. Claims 1, 7, 9, 12, 19, 20, 30 and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by HODGE et al., U.S. Patent No. 3,373,039. HODGE teaches the compounds and compositions of the compounds of formula where X is O; Z is O; A-B is CHR₅-CHR₆ where R₆ is H and R₅ is H; D-E is CHR₈-CHR₉ where R₈ is H and R₉ is H; G-J is CHR₁₀-CHR₁₁ where R₁₀ is H and R₁₁ is H; R₁ is NH₂; R₃ is NH₂; R₂ is OH; R₄ is OH; and K-L is CH₂ as shown by compound XXXIV.

Claim Objections

19. Claims 2, 3, 8, 11, 15-18, 34, 35, 63-66, 71 and 72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Allowable Subject Matter

20. Claims 22, 24-28, 57, 58 and 67-70 are allowed. None of the prior art or record or a search in the pertinent art area teaches the compounds of the instant invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

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Brenda L. Coleman
Primary Examiner Art Unit 1624
April 3, 2005